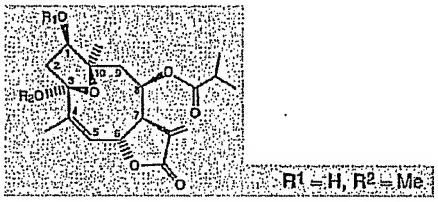
REMARKS

Claims 36-70 are currently pending in this application. The amendments to claims 36-38 are supported at paragraph [0042] "TD-3" (1S,3R,4S,6R,7S,8R,10R)-1-hydroxy-3-methyloxy-3,10-epoxy-8-isobutyryloxygermacra-11(13)-en-6,12-olide, paragraph [0044] "TD-6" (1S,3R,6R,7R,8R,10R)-1-hydroxy-3-methoxy-3,10-epoxy-8-isobutyryloxygermacra-4,11(13)-dien-6,12-olide and paragraph [0043] "TD-5" (4S,5R)-4-hydroxy-4-((1E,3S)-3-hydroxy-1-buteneyl]-3,3,5-trimethyl cyclohexanone, respectively. No new matter has been added to the application by any of the foregoing amendments.

Claim 37 has been rejected under 35 U.S.C. §102(b) as being anticipated by Pereira et al. (Phytochemistry (1997), 45(7), 1445-1448).

Pereira et al. allegedly teaches at page 1446:

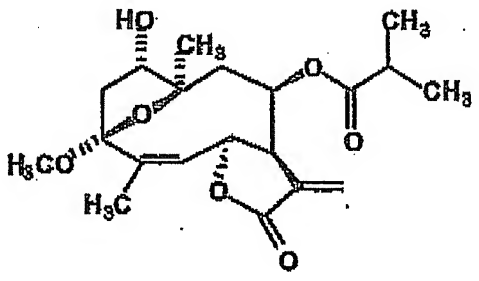


corresponding to the instantly claimed compound of formula II.

Applicants respectfully traverse this §102(b) rejection and request that the rejection be reconsidered and withdrawn.

In order to support an anticipation rejection under 35 U.S.C. §102(b), each and every element of the claimed invention, or its substantial equivalent, must be found within the four corners of a single reference cited by the Examiner to anticipate. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

Claim 37 is directed to the following compound:

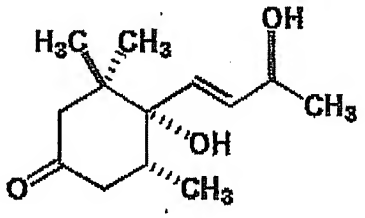


(1S,3R,6R,7R,8R,10R)-1-hydroxy-3-methoxy-3,10-epoxy-8-isobutyryloxygermacra-4,11(13)-dien-6,12-olide, which is stereochemically different from the compound disclosed by Pereira et al. (note the stereochemistry of the hydroxy substituent).

Accordingly, Applicants respectfully assert that claim 37 is novel over the cited compound of Pereira et al. and requests that the rejection be reconsidered and withdrawn.

Claim 38 has been rejected under 35 U.S.C. §102(b) as being anticipated by Gonzalez (Journal of Natural Products (1994), 57(3), 400-2), which allegedly teaches on page 40, column on the right, structure 2, same as the compound of claim 38. The instant claim recites that the 3-hydroxy-1-butenyl is in a 3S-configuration which is opposite of Gonzalez depiction of stereochemistry at C9 (as R). According to the Office Action, Gonzalez's stereochemical assignment was an "assumption" based on biogenetic grounds (see page 401, column 1, last paragraph) coupled with extension of NMR data obtained for blumenol A. Gonzalez's assignment was re-investigated by Calis et al. Phytochemistry (2002), 59, 451-457, resulting in unequivocal assignment for C9 of blumenol as S (see page 453, column 1, line 9). According to the Office Action, comparison of NMR data for compound TD-5, i.e., the compound of claim 38, and that of Gonzalez's compound, shows (see page 21 of the specification), that the instantly reported numbers are shifted by approximately 0.07 ppm, presumably due to NMR measurements at different field strength.

Claim 38 is directed to the following compound:



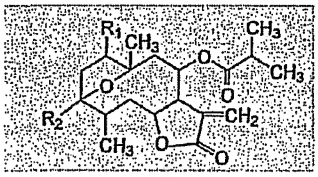
(4S,5R)-4-hydroxy-4-((1E,3S)-3-hydroxy-1-buteneyl]-3,3,5-trimethyl cyclohexanone, which is different from the compound disclosed by Gonzalez. Calis et al. state that an upfield shift of C-9 (ca. 74 ppm) is indicative for the (9S)-configuration whereas compounds with (9R)-configuration exhibit the lower field signal (ca. 77 ppm). The 74 ppm value does not agree with that reported by Applicants at page 21.

Accordingly, Applicants respectfully assert that claim 38 is novel over the cited compound of Gonzalez in view of Calis et al. and requests that the rejection be

reconsidered and withdrawn.

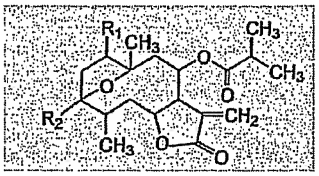
Claim 38 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Baruah et al. (Journal of Organic Chemistry, 1979, (44)11, 1831) in view of Zdero et al. Phytochemistry (1987), 26(7), 1999-2006. It appears that the Office Action intended to reject claim 36, not claim 38, since the structure presented is from claim 38. Applicants will address the rejection with respect to claim 36. If this is incorrect, Applicants request that the undersigned attorney be notified to ensure a compliant response.

Claim 36 (prior to amendment) was drawn to compound:



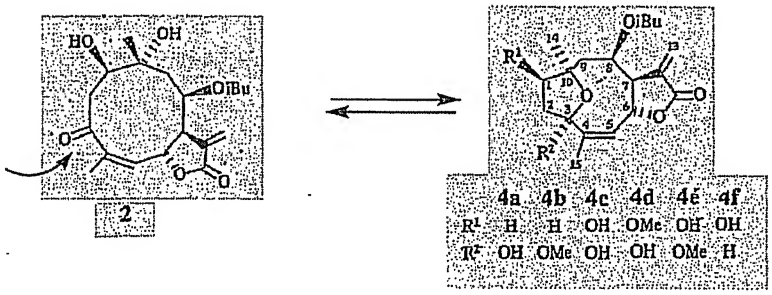
wherein R_1 is hydroxy and R_2 represents methoxy.

According to the Office Action, Baruah et al. allegedly teaches:



wherein R_1 is hydroxy and R_2 represents hydroxy. See structure 7 on page 1832. The difference is the R_2 group in the prior art is hydroxy vs. the R_2 group is methoxy in the compound of claim 36.

The Office Action contends that Zdero et al. teaches the equilibrium shown below.



The equilibrium is between the closed and open position, keto group shown by the arrow and the hydroxyl at C-9, forming hemiketal (and hemiketal-methyl ether) (based on whether water or methanol is present). Further, Zdero et al. states at page 2000, right-hand column, lines 8-9, that the O-methyl ether(s) may be artifacts as methanol was used for extraction (similar to the extraction procedures of the instant application) and that all of these compounds are obviously biogenetically related product (see line 1 of the same paragraph).

The difference between the instantly claimed hemiketal-methyl ether and compounds 4 of Zdero et al. is the double bond between 4-5 positions shown for Zdero's compounds; in the instant case, there is single bond between 4-5 positions. It would be obvious to one of ordinary skill in the art of organic chemistry, that the 4-5 double bond is non-participant in the equilibrium shown above as well as a non-participant in the methyl ether formation. Parallel equilibrium and methyl ether formation is suggested for the compound of Baruah et al. and the compound of the instant claim.

Applicants respectfully traverse this §103(a) rejection and request that the rejection be reconsidered and withdrawn.

As reiterated by the Supreme Court in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. ___, 82 U.S.P.Q.2d 1385 (2007), the framework for the objective analysis for determining obviousness under 35 U.S.C. §103 is stated in *Graham v. John Deere*. Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, 72 Fed. Reg., No. 195 (October 10, 2007) at page 57527 (hereinafter "Examination Guidelines"). The factual inquiries enunciated by the Court are as follows:

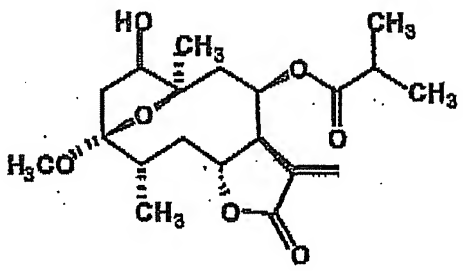
(1) Determining the scope and content of the prior art;

(2) Ascertaining the differences between the claimed invention and the prior art; and

(3) Resolving the level of ordinary skill in the pertinent art.

Examination Guidelines at page 57527.

Claim 36, as amended, is compound represented by general formula (I):



(1S,3R,4S,6R,7S,8R,10R)-1-hydroxy-3-methyloxy-3,10-epoxy-8-isobutyryloxygermacra-11(13)-en-6,12-olide.

Neither Baruah et al. nor Zdero et al., taken together as set forth in the Office Action, suggest or disclose the compound of claim 36, as amended, having the stereochemistry as indicated. Further, the difference between the double bond between 4-5 positions shown for Zdero's compounds vs. the single bond between 4-5 positions of the compound of claim 36 is not a trivial difference as alleged in the Office Action.

Accordingly, Applicants respectfully assert that claim 36 is not obvious over the teachings of Baruah et al. and Zdero et al. and requests that the rejection be reconsidered and withdrawn.

Claims 55 and 70 have been rejected under 35 U.S.C. §103(a) as being unpatentable over prior art references listed in the Office Action at page 6, taken from page 6 of the specification. Claims 55 and 70 are drawn to compounds of claims 36 and 60 respectively, obtained by the process of chromatographic purification/isolation. The Office Action contends that all of these compounds are biogenetically related and are routinely isolated by chromatographic purification, referring to the numerous references cited by the Applicants on pages 6 and 7, as well as references cited by the Office Action drawn to chromatographic separation of these biogenetically and structurally related compounds. The Office Action argues that nothing unobvious is seen in the methods of instant process and the processes of the above-cited references.

Applicants respectfully traverse this §103(a) rejection and request that the rejection be reconsidered and withdrawn.

Claims 55 and 70 are drawn to compounds of claims 36 and 60 respectively, obtained by the process of chromatographic purification/isolation. These compounds are not suggested or disclosed by the references cited in the rejection. The Office Action uses impermissible hindsight reconstruction to construct an argument that claims 55 and 70 are

obvious. The chromatographic purification/isolation of these compounds is not suggested in the cited references.

Accordingly, Applicants respectfully request that the §103 rejection of claims 55 and 70 be reconsidered and withdrawn.

Claims 36-38 have been rejected under 35 U.S.C. §112, second paragraph, for indefiniteness as being drawn to diastereomerically different compounds represented by structural formulae I and II. Thus, for example, in formula I, 128 unique compounds are possible. It is unclear what compound the applicant is seeking protection for. The Office Action notes that in claim 38, Applicants specifically refer to stereochemically defined structure to negate possible rejections of this claim under 35 U.S.C. §102(b).

For similar reasons, claims 36-37 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for two compounds, allegedly does not reasonably provide enablement for over 200 compounds claimed. The Office Action contends that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims are drawn to many structurally, complex, but biogenetically-related compounds (see above rejection under 35 U.S.C. §112, second paragraph). Since no synthetic methods or methods of interconverting and or isomerizing existing stereocenters are presented in the specification, the Office Action alleges that it is clear that the presently claimed compounds are from natural sources. According to the Office Action, because the (enzymatic) nature of biosynthesis is inherently stereospecific, it provides only one stereoisomer alleging that there are very few, if any, exceptions found in this class of compounds. Because of this elegance of nature, the number of conceivable compounds in the instant case is limited to one for each formula. As such, the disclosure in the specification is not commensurate with the breadth of the claims.

Applicants respectfully traverse these §112 rejections and request that the rejections be reconsidered and withdrawn.

Claims 36-38 have been amended to clarify the stereochemistry of the claimed structures. These structures are supported at paragraph [0042] "TD-3" (1S,3R,4S,6R,7S,8R,10R)-1-hydroxy-3-methyloxy-3,10-epoxy-8-isobutyryloxygermacra-11(13)-en-6,12-olide, paragraph [0044] "TD-6" (1S,3R,6R,7R,8R,10R)-1-hydroxy-3-methoxy-3,10-epoxy-8-isobutyryloxygermacra-4,11(13)-dien-6,12-olide and paragraph

[0043] "TD-5" (4S,5R)-4-hydroxy-4-((1E,3S)-3-hydroxy-1-buteneyl]-3,3,5-trimethyl cyclohexanone, respectively. Accordingly, Applicants respectfully request that the §112 rejections be reconsidered and withdrawn

Also, Applicants respectfully request that the Information Disclosure Statements filed on June 26, 2008 and January 17, 2008 be considered and entered into the file record.

In view of the foregoing amendment and remarks, allowance of claims 36-70 is respectfully requested.

Respectfully submitted,

THE WEBB LAW FIRM

Date August 25, 2008

By _____

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